D-glucuronic acid coated $DyEuO_3$ and $HoEuO_3$ nanoparticles for magnetic resonance imaging (MRI) and fluorescence imaging (FI)

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Introduction

A dual imaging now emerges as a new and advanced imaging technique in clinical applications. The single-phase mixed $DyEuO_3$ and $HoEuO_3$ nanoparticles are potential candidates for dual imaging experiment. It is expected that it will play a key role to diagnose diseases by replacing conventional single-imaging techniques. For example for MRI-FI dual imaging, the fluorescence imaging can be used to locate a disease and then MRI can be used to obtain high resolution MR images around the disease. We developed a facile synthesis of ultra-small D-Glucuronic acid coated Eu^{3+} doped Dysprosium oxide nanoparticles and Holmium oxide nanoparticles. It was well characterized by using MP-XRD, TEM, FT-IR spectrophotometer, TGA, photoluminescence spectrophotometer, SQUID magnetometer and Magnetic Resonance Imaging (MRI) instrument. The nanoparticles were found monodisperse and average particle diameter is estimated to be ~4 nm. The capability of nanoparticles as T_2 MRI contrast agent was proved in vivo through T_2 MR images of a rat. The fluorescent images were observed in vitro by taking DU145 and NCTC1469 cells. The $DyEuO_3$ and $HoEuO_3$ nanoparticles were found to be paramagnetic and emitted red fluorescence. The nanoparticles exhibited no appreciable cytotoxicity up to 100 µM concentrations and in vivo MR experiment showed the negative contrast enhancement on mouse liver and kidneys after the injection of nanocolloid. Hence, it can be used as a fluorescence imaging agent as well as a T_1 MRI contrast agent.

Materials and methods

4 mmol of $Dy(NO_3)_3.5H_2O$ and 1 mmol of $Eu(NO_3)_3.5H_2O$ was added to 40 mL triethylene glycol in a three neck flask and magnetically stirred at 40 °C until the precursor was dissolved. After that 6 mmol of NaOH was added to the methanol l solvent on refluxing at 40 °C with magnetic stirring until the NaOH was dissolved. Then we add it to the precursor mixture, and increase the temperature on 200 °C to refluxe for 24 h, gives $DyEuO_3$ nanoparticles. After decreasing temperature to room temperature, D-Glucuronic acid is added. After refluxing for 24 h on 80 °C, ultrasmall mixed dysprosium-europium oxide nanoparticles were given.

Result and Discussion:

HRTEM images show that the diameter (d) of the $DyEuO_3$ nanoparticles in its nanocolloid is nearly monodisperse and ranges from 3 to 5 nm (fig.1). The surface coating of nanoparticles by D-Glucuronic acid was confirmed by recording a FT-IR absorption spectrum of a powder sample. The amount of surface coating of the $DyEuO_3$ nanoparticle with the D-Glucuronic acid in nanocolloid were estimated to be 51.0% by recording a TGA curve of a powder sample. It shows that the nanoparticles are sufficiently coated with the D-Glucuronic acid. To characterize magnetic properties of the nanoparticles in the $DyEuO_3$ nanocolloid, both M-H and ZFC M-T curves and were recorded. The M-H curves show that both coercivity and remanence are zero. This lack of hysteresis as well as no magnetic transition down to T =3 K in the ZFC M-T curve shows that the nanoparticles are mainly paramagnetic down to T =3 K. From the M-H curve at T =5 K and at T=300 K, magnetizations of the $DyEuO_3$ nanoparticles were estimated to be ~ 117.6 emu/g. The PL spectrum of D-Glucuronic acid coated $DyEuO_3$ nanoparticles is shown in figure 5. The observed peaks at 583 nm in the sample solution are due to the emission from $^5D_0$ to $^7F_0$. Among these emission peaks, the third one corresponds to the principle emission. The R_1 and R_2 map images clearly showed dose dependent contrast changes with increasing the dose (fig.2). The r_1 and r_2 relaxivities of 0 and 82.5 s^{-1} mM^{-1} were obtained from the slopes in the plots of R_1 and R_2 relaxivities as a function of Dy concentration respectively (fig.3). For the $DyEuO_3$ nanocolloid to be safely applied in vivo, it should be nontoxic. We performed an *in vitro* cytotoxicity test of the nanocolloid by using the human prostate cancer (DU145) cell lines and (NCTC 1469) cell lines as shown in fig.4. The $DyEuO_3$ nanocolloid is not toxic for the tested concentration range up to 100 µM Dy. In vivo MR images were recorded which showed the increase of contrast enhancement on kidney of mouse after 1 h of injection of MRI solution. Hence, it can be inferred that ultrasmall single phase $DyEuO_3$ nanoparticles can be used as a dual imaging probes.

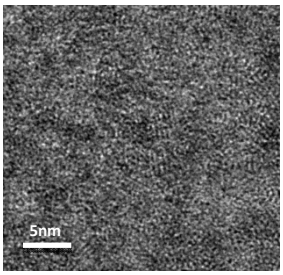

Fig. 1 HRTEM image

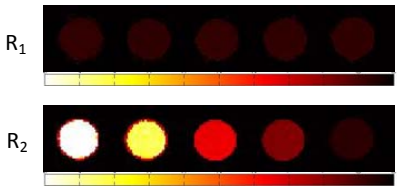

Fig. 2 Map images

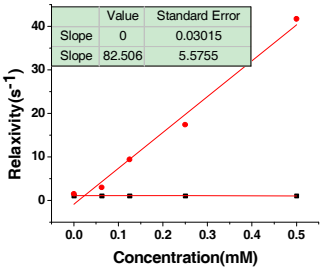

Fig. 3 Measurement of Relaxivity

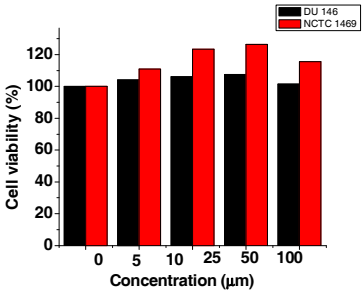

Fig. 4 *In vitro* cytotoxicity test

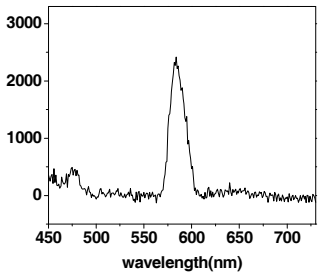

Fig. 5 PL spectra by excitation 430nm

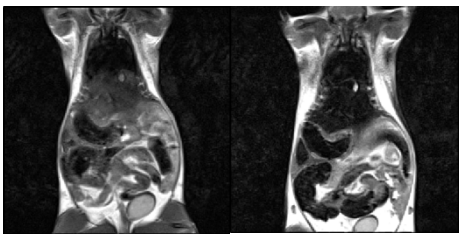

Fig. 6 *In vivo* MR images (Mouse kidney)